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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,387	03/26/2001	Eckart Matthes	101195-24	9650

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
12/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/817,387	MATTHES ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-7,9-11 and 16-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,7,9-11 and 16-22* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09423157.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10-09-2007 has been entered.

Response to Arguments

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. 1, 2, 5-7, 9-11 and 16-22 are presently pending in the instant application.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 9-11, 17, and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Instant claim 9 recites the oligonucleotide of claim 1, wherein the oligonucleotide is bound to telomerase. Moreover, claims 10-11 and claim 17 recite the oligonucleotide of claim 1, wherein the oligonucleotide is bound to telomerase. The metes and bounds of these claims are vague and indefinite since it is unclear if the instant claims are

merely drawn to the oligonucleotide of claim 1, wherein the oligonucleotide is capable of binding to a telomerase protein, or if these claims are drawn to an oligonucleotide, further comprising wherein the oligonucleotide is bound to telomerase in a complex, such that the claim is actually directed to the complex of the oligonucleotide bound to the telomerase protein, or further wherein the claim is drawn to a complex comprising the oligonucleotide claim 1 that is bound to an RNA component of the telomerase protein (see claim 17). Moreover, the metes and bounds of claims 10-11 are vague and indefinite since it is unclear if the instant claims are drawn to merely the oligonucleotide of claim 1, or to a complex comprising an oligonucleotide, a telomerase, and a cell.

7. Claim 19-20 are also rejected to the extent that the nature of the claimed invention is unclear. For example, claims 19-20 recite an oligonucleotide according to claim 1 bound non-specifically to a protein site. First, as recited above, it is unclear if the instant claims are drawn to the oligonucleotide of claim 1, or to a complex comprising said oligonucleotide of claim 1, and further wherein said oligonucleotide is bound to a protein.

8. In regards to claim 21, it is unclear if the claim is drawn to a single oligonucleotide of claim 1, or multiple since the claim recites "oligonucleotides of claim 1." Moreover, it is unclear if the instant claim is directed to the oligonucleotide only, or to a complex comprising said oligonucleotide and a cationic liposome.

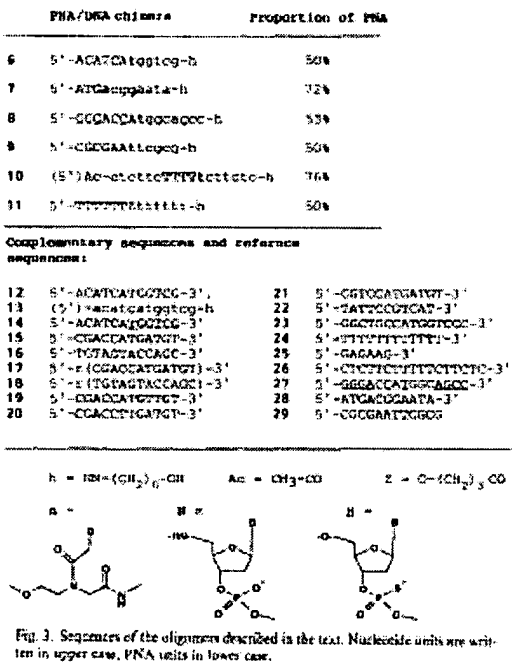
Claim Rejections - 35 USC § 103

9. Applicant's arguments with respect to claims 1-2, 5, 7, 9-11, 17-20, and 22 have been considered but are moot in view of the new ground(s) of rejection. Moreover, the

opinions presented in the Affidavit under 37 CFR 1.132 filed 10/09/2007 are addressed to some extent as they read on the new grounds of rejection set forth below.

10. Claims 1-2, 5, 7, 9-11, 17-20, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uhlmann et al. and Nielsen et al. (US Patent No. 5,539,082) et al. in view of Norton et al. (1996) and Mata et al.

11. Uhlmann et al. teach the synthesis and properties of PNA and DNA chimeras of any desired sequence by an automated synthesizer. In one particular embodiment, Uhlmann et al. disclose compounds of the following structure:



	PNA/DNA chimera	Proportion of PNA
6	5'-ACATCAtggtcg-h	50%
7	5'-ATGaggaata-h	72%
8	5'-GCGACCAtgccagcc-h	53%
9	5'-CGCGAAttcgcg-h	50%
10	(5')Ac-etottcTTTTtcttctc-h	76%
11	5'-TTTTTTttttt-h	50%

Complementary sequences and reference sequences:

12	5'-ACATCATCGTCG-3',	21	5'-CGTCGATGATGT-3'
13	(5')-acatcatggtcg-h	22	5'-TATTCCTTCAT-3'
14	5'-ACATCATGGTCG-3'	23	5'-GGCTGGCATGGTCGC-3'
15	5'-CGACCATGATGT-3'	24	5'-TTTTTTTTTTTT-3'
16	5'-TGTAGTACCAGC-3'	25	5'-GAGAAG-3'
17	5'-z(CGACCATGATGT)-3'	26	5'-CTCTTCTTTTTCTTCTC-3'
18	5'-z(TGTAGTACCAGC)-3'	27	5'-GGGACCATGGTAGCC-3'
19	5'-CGACCATGTTCT-3'	28	5'-ATGACGAATA-3'
20	5'-CGACCTTGATGT-3'	29	5'-CGCGAATTCGCG

h = $NH-(CH_2)_6-OH$ Ac = CH_3-CO z = $O-(CH_2)_5-CO$

Fig. 3. Sequences of the oligomers described in the text. Nucleotide units are written in upper case, PNA units in lower case.

In compound **8** above we see underlined nucleotides, these correspond to nucleotides having phosphorothioate linkages in the 5' portion of the molecule, and having PNA oligomers on the 3' end of the structure. The oligonucleotide also comprises a 3' terminal amino group comprising an acid labile protecting group. However, Uhlmann et

al. does not teach wherein **n** is at least 10 and not more than 20, and **p** is at least 3 and not more than 17. Moreover, Uhlmann et al. does not teach wherein this structure inhibits the activity of telomerase, or wherein the chimeric oligonucleotide structure comprises a terminal amino group.

Nielsen et al. teach the following concluding step in the synthesis of peptide nucleic acid:

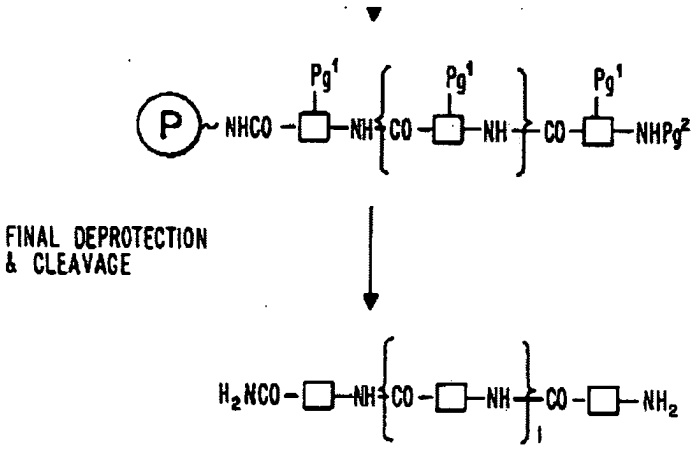


FIG. 1

Norton et al. teach the inhibition of human telomerase activity by peptide nucleic acids (PNAs). According to Norton et al. PNAs recognize the RNA component of human telomerase (hTR) and inhibit activity of the enzyme. Inhibition depends on targeting exact functional boundaries of the hTR template. Norton et al. also observed that phosphorothioate (PS) oligomers inhibit telomerase in a non-sequence selective fashion. Additionally, Mata et al. teach that hexameric phosphorothioate oligomers function to inhibit telomerase activity and arrests growth of Burkitts lymphoma cells.

It would have been obvious to the ordinary skilled artisan to combine the teachings of the above-cited references in the design of the present invention. Absent evidence of any unexpected results, one of ordinary skill in the art would have been motivated to make the oligomers of the present invention to comprise wherein **n** is at least 10 and not more than 20, and **p** is at least 3 and not more than 17, since the Uhlmann et al. clear teach that chimeric PNA/DNA oligonucleotides or any sequence can be readily prepared, and Norton et al. discloses the nucleotide structure of an oligomer (15 base pairs in length; i.e. satisfying **n** and **p**) that recognizes the RNA component of human telomerase and inhibits the activity of the enzyme. Absent evidence of unexpected results, since the general conditions of the claimed invention are disclosed in the prior art, the recitation of the limitations "wherein n is at least 10 and not more than 20, and p is at least 3 and not more than 17," merely represents a difference of merely a design choice.

Furthermore, in regards to the presence of a terminal primary amino group in the PNA oligomeric chimeras, it is noted that the compounds of Uhlmann et al. disclose a secondary amino group at the end of their chimeras, it is noted that the terminal secondary amino group in the compounds of Uhlmann et al. comprises an acid labile protecting group, which can readily be converted to a primary amino group via cleavage of the protecting group after synthesis is complete as per the teachings of Nielsen et al. Nielsen et al. clearly teach the synthesis of PNA oligomers comprising a terminal amino group.

Moreover, in regards to the Affidavit filed under 37 CFR 1.132, inventor argued that the above statements has no scientific basis, however Applicant's statement was not supported by any scientific evidence to disprove the assertions made by the examiner. It is clear that the prior art teaches the design of chimeric oligonucleotides for the express purpose of inhibiting telomerase activity, Applicant's own specification makes mention of the Uhlmann et al. reference cited above (see page 9, last ¶ of specification filed 3/26/2001) which recites: "Phosphorothioate is linked with PNA according to described methods, if necessary with using linkers (Uhlmann, E. et al. Ange. Chem. (1996) 18, 2793-2797)."

Furthermore, in regards to Applicant's assertion at ¶ #18 of the Affidavit filed 10/09/2007, ("None of the cited references disclosed, proposed, or synthesized such chimeric ODN because it is not obvious without our findings to propose and to synthesize such novel telomerase tailor-made chimeric ODN. For this reason it would not have been obvious to combine the cited references.)" Although, Applicant's finding that phosphorothioate oligonucleotides competitively bind to the primer binding site of the telomerase enzyme is significant, this feature is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Furthermore, in regards to the presence of the primary amine at the 3' terminus of the claimed PNA chimeric structures, it is noted that the claimed chimeric oligonucleotides of formula III does not recite a primary amine function, therefore the

significance of this structure as asserted by Applicants in paragraph #19 of the Affidavit is not consistent with the scope of the claimed invention. The absence of the 3' terminal amine group in formula III, suggests that the activity of the claimed oligonucleotides would not be greatly influenced by the presence and/or absence of an amine function at the 3' end.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 5, 9-11, 19-21, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Iversen et al. ((WO 96/23508 A1).

It is noted that the prior art is applied to the extent that claims 9-11 and 19-21 are interpreted as reading on the oligonucleotide as recited in claim 1.

Iversen et al. discloses oligonucleotides that for inhibiting proliferation of cancer cells comprising delivering an oligonucleotide comprising a nucleotide sequence which mimics a telomere repeat motif, wherein the oligonucleotide has a phosphorothioate backbone modification (see page 21, example 5 which discloses an 18-mer having 92% inhibition, Table 2). See also, for example, the phosphorothioate oligonucleotide having the following structure: 5'-d(TTAGGG)$_3$-3', absent evidence to the contrary, this structure meets all the limitations of the instant claims to the extent that they read on oligonucleotides of formula III.

14. Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE